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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/163,089	09/29/98	MCKENZIE I	4102-1

022442
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HM22/0213

EXAMINER	
SIU,S	
ART UNIT	**PAPER NUMBER**
1631	15

DATE MAILED: 02/13/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/163,089	Applicant(s) MCKENZIE ET AL.	
	Examiner Stephen Siu	Art Unit 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 January 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,19-22,24-46 and 48-51* is/are pending in the application.

4a) Of the above claim(s) *2,22,24,35 and 46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3-17,19-21,25-34,36-45 and 48-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

This is in response to Applicant's amendment received January 2, 2001 (paper number 14).

The rejection of claims 11, 12, and 25 under 35 U.S.C. 112, second paragraph as cited in the office action mailed July 23, 2000 (paper number 12) is withdrawn in view of Applicant's arguments and amendments.

The rejection of claims 18, 23, and 47 under 35 U.S.C. 112, first paragraph as cited in the office action mailed July 23, 2000 (paper number 12) is withdrawn in view of cancellation of the claims.

The rejection of claims 1, 3-16, 17-21, 23-27, 32-34, 36-40, 43-45 and 47-50 under 35 U.S.C. 103(a) as being unpatentable over Rodwell in view of Edelsen and in further view of Kjeldsen as cited in the office action mailed July 23, 2000 (paper number 12) is withdrawn in view of Applicant's arguments and amendments.

The rejection of claims 1, 3-21, 23-27, 32-34, 36-40, 43-45, and 47-50 under 35 U.S.C. 103(a) as being unpatentable over Taylor-Papadimitriou in view of Rodwell and in further view of Edelsen as cited in the office action mailed July 23, 2000 (paper number 12) is withdrawn in view of Applicant's arguments and amendments.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 13-16 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention as cited in the office action mailed July 28, 2000 (paper number 12) is maintained. Claim 13 has been amended to recite an antigenic fragment of at least 5 amino acids in length.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must provide an antigenic peptide fragment of at least 5 amino acids in length. For the reasons discussed below, there would be an unpredictable amount of experimentation required to practice the claimed invention.

b) The specification presents only general guidance for providing fragments of MUC1 to MUC7, on which antigenic fragments could be based (pages 3-4), fragments of mucin that could be used (pages 25-26). Of note is that MUC1 to MUC7 are longer than 5 amino acids in length. Although the specification provides a suggestion of the

possibility that MUC1 to MUC7 fragments might be used, the specification does not present specific data for ensuring the antigenicity of the claimed fragments that are 5 amino acids in length in such a way that an antigenic peptide fragment of 5 amino acids in length would be predictably achieved. The specification provides guidance to test the antigenicity of a given peptide fragment but does not disclose the claimed antigenic peptides of 5 amino acids in length.

c) The specification does not provide working examples of the claimed antigenic peptides of 5 amino acids in length such that the peptides would be predictably antigenic.

d) The invention is drawn to antigenic peptides of 5 amino acids in length.

e) Abbas (Cellular and Molecular Immunology, Chapter 6, Antigen presentation and T Cell Antigen Recognition, 1991, page 131) teaches that amino acid sequences must be 10-20 amino acids in length for effective Class I MHC-associated antigen presentation and antigenicity because each class 1 MHC molecule has a single binding cleft that accommodates peptides that are 10 to 20 amino acids long (page 131, col.1).

f) The skill of those in the art of molecular biology is high.

g) The prior art predicts that a peptide that is 5 amino acids in length would not be antigenic because class 1 MHC molecules would not accommodate peptides 5 amino acids in length.

h) The claims read broadly on amino acid fragments of at least 5 amino acids in length.

The skilled practitioner would first turn to the instant specification for guidance in practicing the claimed invention. However, the specification does not provide specific guidance or working examples to practice the claimed invention. The specification provides guidance to provide amino acid sequences that might be used but does not demonstrate that the amino acid sequences would predictably be antigenic. As such, the skilled practitioner would next turn to the prior art for such guidance, however the prior art shows failure in antigenicity of peptides that are 5 amino acids in length because class 1 MHC molecules accommodate peptides that are 10 to 20 amino acids in length but not 5 amino acids in length. Finally, said practitioner would turn to trial and error experimentation without guidance from the specification or the prior art to practice the claimed method of providing an antigenic peptide of 5 amino acids in length. Such represents undue experimentation.

Applicant's arguments filed January 2, 2001 (paper number 14) have been fully considered but they are not persuasive. Applicant maintains that a skilled artisan would supposedly be able to determine immunogenic peptides 5 amino acids in length given the disclosure of MUC1 to MUC7 on pages 3-4 of the specification and amino acid sequences disclosed on pages 25-26 of the disclosure. However, the disclosed sequences are all greater than 5 amino acids in length and no disclosure demonstrates immunogenic peptides of 5 amino acids in length. The prior art teaches peptides of 5 amino acids in length as being non-immunogenic as described above. Thus, the specification does not enable one of skill in the art to provide immunogenic peptides of 5 amino acids in length. Applicant further states that a skilled artisan would be able to test

peptide fragments for immunogenicity. However, the claims are drawn to immunogenic peptide fragments that are 5 amino acids in length. As such, the claimed invention is not disclosed in the specification as demonstrated by the fact that the skilled artisan would be required to undergo laboratory testing on 5 amino acid fragment and substring to determine immunogenicity. Further, the prior art predicts failure of immunogenicity of amino acid fragments that are 5 amino acids in length indicating that the skilled artisan would not be able to find any immunogenic fragments of 5 amino acids in length even if the skilled artisan were to perform such lengthy and arduous experimentation. Thus, this would constitute undue experimentation to the skilled artisan.

The rejection of claims 1, 3-21, 23-34, 36-45 and 47-51 under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention is maintained.

In *In re Wands* (8 USPQ2d 1400 (CAFC 1988)) the CAFC considered the issue of enablement in molecular biology. The CAFC summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the breadth of the claims.

In considering the factors for the instant claims:

a) In order to practice the claimed invention one of skill in the art must provide an immunoregulatory composition comprising an antigen and a carbohydrate polymer comprising at least one mannose. The claims are not limited to an immunoregulatory compostion comprising mannose or mannan. For the reasons discussed below, there would be an unpredictable amount of experimentation required to practice the claimed invention.

b) The specification presents only general guidance for providing an immunoregulatory composition comprising mannose on page 7, lines 10-12, lines 21-22, and binding studies with mannan, oxidized mannan and reduced mannan (page 49, table 1). The specification does not present specific data for all carbohydrate polymers containing one mannose in such a way that an immunoregulatory composition would be predictably.

c) The specification does not provide working examples of the claimed method of providing an immunoregulatory composition comprising any carbohydrate polymer with one mannose.

d) The invention is drawn to an immunoregulatory composition comprising an antigen and any carbohydrate polymer with one mannose.

e) The prior art does not teach an immunoregulatory composition comprising mannose receptor-bearing cells and a conjugate comprising an antigen and any carbohydrate polymer with one mannose.

f) The skill of those in the art of molecular biology is high.

g) The prior art does not provide guidance for utilizing any carbohydrate polymer containing one mannose in an immunoregulatory composition comprising isolated mannose receptor-bearing cells..

h) The claims read broadly on an immunoregulatory composition comprising a conjugate comprising an antigen and any carbohydrate polymer containing one mannose rather than merely on a conjugate comprising mannan..

The skilled practitioner would first turn to the instant specification for guidance in practicing the claimed invention. However, the specification does not provide specific guidance or working examples to practice the claimed invention. The specification provides guidance to provide an immunoregulatory composition comprising a conjugate containing mannan but does not provide guidance to provide an immunoregulatory composition comprising a conjugate containing any carbohydrate polymer with one mannose. As such, the skilled practitioner would next turn to the prior art for such guidance, however the prior art does not provide guidance in the use of any carbohydrate polymer with one mannose. Finally, said practitioner would turn to trial and error experimentation without guidance from the specification or the prior art to practice the claimed method of gene therapy. Such represents undue experimentation.

Applicant's arguments filed January 2, 2001 (paper number 14) have been fully considered but they are not persuasive. Applicant asserts that the carbohydrate polymers are not a single mannose but are carbohydrate polymers comprising mannose. However, the specification only provides guidance and working examples of mannan and does not provide guidance for any carbohydrate polymer with at least one

mannose. Thus, the skilled practitioner would not be enabled to perform the claimed invention with any carbohydrate polymer with one mannose through the disclosure of the present application without undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and dependent claims 2-19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 (and dependent claims 2-19) recite "a conjugate comprising an antigen and a carbohydrate polymer comprising mannose selected from the group..." which is confusing because it is not clear if the Markush group refers to the mannose or the carbohydrate polymer.

Conclusion

No claims allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, this Action is made final. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Stephen Siu, whose telephone number is (703) 308-7522. The Examiner can normally be reached from 7:00 a.m. to 3:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Michael Woodward, can be reached at (703) 308-4028. Papers related to this application may be submitted to Art Unit 1631 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If applicant does submit a paper by FAX, the original copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office. The Fax number is (703) 308-0294. Please call the Examiner at (703) 308-7522 before the transmission to expedite delivery of the fax. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Stephen Siu

JOHN S. BRUSCA, PH.D
PRIMARY EXAMINER